The current role of radiotherapy in paraplegia due to extramedullary hematopoiesis in thalassemia: A case report and a review of the literature.

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ABSTRACT: Spinal cord compression as a consequence of mass lesions due to extramedullary hematopoiesis is a well-described but rare syndrome occurring in thalassemia and some other hematologic conditions. Generally presents as paraparesis with sensory impairment. Treatment option mostly includes surgery and/or radiotherapy. After low-dose radiotherapy a rapid and durable response occurred in a patient with thalassemia. No side effects were encountered and the patient has been stable neurologically. We hereby report a case of thalassemia with paraplegia treated successfully with low-dose radiotherapy.

Key Words: Thalassemia, Extramedullary hematopoiesis, Cord compression, Radiation therapy.

INTRODUCTION

Extramedullary hematopoiesis (EMH) is a rare compensatory process associated with many hematologic disorders and bone marrow dysfunction. EMH commonly involves the liver, spleen and lymph nodes. Normally, it occurs in the marrow of long bones, the ribs, and the vertebrae of an adult. EMH is described as an ectopic production of myeloid, erythroid, and megakaryocytic elements. Ectopic production is believed to be a compensatory mechanism that is subsequent to bone marrow stress and inability to compensate for the body’s hematologic demands. Histologically, EMH typically mimics normal bone marrow. Spinal cord compression due to EMH is an extremely rare complication. A few reports have described patients with complete paraplegia and none patient has been treated only with radiotherapy. We present a case of a patient of thalassemia with paraplegia treated successfully with radiotherapy.

CASE REPORT

A 32-year-old male presented with an 8 month history of parasthesias and weakners of both lower limbs and progressive sphincter disturbances. He was diagnosed as case of thalassemia at the age of 3 when he was found with a hemoglobin level of 7 g/dL, following a febrile episode. Physical examination revealed a young male with a height of 160 cm and weighing 42 kg with poor muscular development. Magnetic resonance imaging (MRI) of the spine showed extradural and paravertebral masses extending from T5 to T7 and L5 to I1, causing cord compression. The appearance of the masses along with the known underlying hematological condition was strongly suggestive of EMH. A neurosurgical opinion was sought, but the patients was opined to be a poor candidate for surgical decompression in view of large extent of lesion, risk of spinal instability due to severe osteoporosis, possibility of hemorrhage and hemodynamic instability.
due to anemia. He was planned for radiation therapy to the involved region of the spine, T₉ - T₇ and L₅ - I₁.

He received a total dose 800cGy (100cGy/fraction) delivered by a linear accelerator 16MV using three fields with dose prescribed at a depth of 6cm for T₉ - T₇ and 7cm for L₅ - I₁. He was also received oral sol. Dexamethasone 20ml x 2per.os everyday, during radiotherapy, for prevention of the after radiation edema in the corresponding irradiated regions. Bilateral lower extremity power improved to grade 4/5 after the third fraction of radiotherapy and 5/5 after the end of treatment. He also regained sphincter control and sensations by the end of treatment. MRI of the spine after 3 months of irradiation showed increased reduction of paravertebral masses extending from T₅ to T₇ and I₁ to I₄.

**DISCUSSION**

Extramedullary hematopoiesis (EMH) can occur in many disorders including thalassemias, polycythemia rubra vera, myelofibrosis, hemolytic anemia and other hemoglobinopathies. Spinal cord compression due to EMH in thalassemia was first reported by Gatto in 1954⁴. Most cases present with paraparesis, sensory impairment and occasionally sphincter disturbances. Complete paraplegia has been reported very rarely in thalassemia and occurs more frequently in polycythemia rubra vera and sickle cell anemia¹. The diagnostic procedure of choice is magnetic resonance imaging (MRI) which characteristically shows an isointense mass with a high spinal intensity rim on T₁ - weighted images and a hyperintense mass on T₂ - weighted images⁵,⁸. Treatment options for cord compression are surgery, radiation therapy, blood transfusions, hydroxyurea or various combinations of them. Radiation therapy has proven to be a very effective modality for treatment of this rare disease as the hematopoietic elements are exquisitely radiosensitive. It has recently been reported that radiotherapy can alone provide complete neurologic recovery in 70% of cases⁶,⁷. Also some authors believe that radiation therapy may cause initial worsening of symptoms due to tissue edema. However, this can be easily prevented or controlled with concomitant steroid therapy⁹. Radiation can also produce marked myelosuppression in a few patients due to a decrease in the extramedullary hematopoietic tissue (upon which they are dependent for blood cell production) or secondary to irradiation of the normal bone marrow in the spine. Hemopoietic tissue is extremely sensitive to radiation and low doses cause rapid shrinkage. In cases of EMH with compression in thalassemia, improvement is clinically evident after an average of three fractions of radiotherapy and near complete recovery is generally observed by the end of treatment¹⁰. Doses used have ranged from 750-3500cGy³. Papavasiliou et al. reported the treatment of 32 patient with 6-26Gy in 1-2.5Gy/Fr, although in a few cases a single fraction of 6Gy was administered¹¹. Munn et al. also found a therapeutic dose range of 15-30Gy after a review of literature⁴.

Plataniotis et. al recently suggested that a total radiation dose in the range of 10-25Gy usually evokes a durable remission and improvement of symptoms. With the availability of CT simulation/treatment planning and MRI, radiation ports can be better limited to the sites of involvement to achieve a satisfactory clinical response with less toxicity to surrounding normal tissues. With these low doses, the only significant toxicity that may occur is a further decrease in blood cell counts which need to be frequently monitored². Excellent results have been obtained in cord compression due to EMH in thalassemia with radiotherapy alone. Our patient showed rapid and near complete recovery with radiation therapy alone despite having long standing paraparesis and paraplegia. Therefore, we conclude that radiation therapy may be the optimal therapeutic approach in such cases.

**CONCLUSION**

Extramedullary hematopoiesis (EMH) is a rare compensatory process associated with many hematologic disorders and bone marrow dysfunction. In cases of paraplegia due to EMH there seems to be a bias towards surgical approach with the aim of causing rapid decompression. Surgery may be associated with various complications including bleeding, hemodynamic instability, spinal instability etc. Radiation therapy is a simple, safe and effective approach for the treatment of spastic paraplegia consequent to spinal cord compression due to EMH¹². Radiation therapy has proven to be an effective modality for treatment of this rare radiosensitive disease.
Ο θεραπευτικός ρόλος της ακτινοθεραπείας στην παραπληγία εξαιτίας της εξωμυελικής αιμοποίησης στη θαλασσαιμία. 
Μια ειδική αναφορά και ανασκόπηση της βιβλιογραφίας.

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ΠΕΡΙΛΗΨΗ: Η πίεση του νωτιαίου μυελού ως αποτέλεσμα κάκωσης από μάζα εξαιτίας εξωμυελικής αιμοποίησης περιγράφεται καλά αλλά είναι ένα σπάνιο σύνδρομο που εκδηλώνεται στη θαλασσαιμία και σε μερικές άλλες αιμολογικές συνθήκες. Γενικά εμφανίζεται ως παραπάρεση με αισθητικές αδυναμίες. Η θεραπευτική αντιμετώπιση περιλαμβάνει το χειρουργείο και/ή την ακτινοθεραπεία. Μετά από χορήγηση μόνο ακτινοθεραπείας σε χαμηλή δόση, σε ασθενείς με θαλασσαιμία, εμφανίστηκε γρήγορη ανταπόκριση με διαρκή αποτελέσματα. Δεν παρατηρήθηκαν παρενέργειες και οι ασθενείς ήταν νευρολογικά σταθεροί. Διά του παρόντος αναφέρουμε μια περίπτωση με θαλασσαιμία και παραπληγία που θεραπεύτηκε με επιτυχία με χορήγηση μόνο χαμηλής δόσης ακτινοθεραπείας.

Λέξεις Κλειδιά: Θαλασσαιμία, Εξωμυελική αιμοποίηση, Πίεση νωτιαίου μυελού, Ακτινοθεραπεία.

REFERENCES